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510(k) Summary of Safety and Effectiveness for the ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment Assay

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

A. 510(k) Number: K110934

B. Date of Preparation: July 8, 2011

C. Proprietary and Established Names:
ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment Assay

D. Applicant

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E. Regulatory Information:

1. Regulation section:
   21 CFR §864.7470, Glycosylated hemoglobin assay
2. Classification:
   Class II
3. Product Code:
   LCP
4. Panel:
   Hematology (81)

F. Predicate Device:

1. Device Name:
   ADVIA® Chemistry Hemoglobin A1c (A1c)
2. Common Name:
   ADVIA® Chemistry Hemoglobin A1c (A1c)
3. 510(k) Number:
   k081895
4. Manufacturer:
   Siemens Healthcare Diagnostics Inc.

G. Intended Use:

For *in vitro* diagnostic use in the quantitative determination of Hemoglobin A1c, a diabetes marker, in whole blood on the ADVIA Chemistry systems. Such measurements are used for monitoring the long-term care of persons with diabetes. The A1c_3 and total hemoglobin

(tHb_3) values generated as part of the ADVIA Chemistry HbA1c% and HbA1cR assays are intended for use in the calculation of the A1c/total hemoglobin ratio, and must not be used individually for diagnostic purposes.

H. Device Description:
The concentration of A1c and the concentration of total hemoglobin are measured and their ratio is reported. The automated pretreatment assays (ADVIA Chemistry A1c_3 and ADVIA Chemistry tHb_3) use 3 ADVIA Chemistry reagents:

- A1c_3 Agglutinator/Total Hemoglobin Reagent (A1c_3 R1)
- A1c_3 Antibody Reagent (A1c_3 R2)
- A1c_3 Denaturant Reagent (A1c_3 DENAT)

I. Test Principle:
HbA1c is formed by the non-enzymatic glycation of the N-terminus of the ß-chain of hemoglobin A. The level of HbA1c is proportional to the level of glucose in the blood and is widely accepted as an indicator of the mean daily blood glucose concentration over the preceding 2 months. Recent studies have shown that the regular measurement of HbA1c leads to changes in diabetes treatment and improvement of metabolic control as indicated by a lowering of HbA1c values.

In an automated pretreatment step, the whole blood sample is mixed with the A1c_3 Denaturant Reagent. The red blood cells are lysed and the hemoglobin chain is hydrolyzed by the protease present in the reagent. For the measurement of total hemoglobin, the A1c_3 Agglutinator Reagent (A1c_3 R1) is used. The assay is based on the determination of released heme in the Soret region at 410 nm.

A latex agglutination inhibition assay is used for the measurement of specific A1c. A second protease in the R1 reagent further hydrolyzes the HbA1c sample to a glycated pentapeptide, which competes with the agglutinator (synthetic polymer containing multiple copies of the immunoreactive portion of A1c) for the anti-HbA1c antibody, thereby reducing the rate of agglutination. A concentration curve is obtained by monitoring the change in scattered light at 694 nm as a change of absorbance. The actual change in absorbance is inversely proportional to the concentration of A1c in the sample.

The A1c_3 and tHb_3 results use the HbA1c% Ratio to determine HbA1c results in NGSP equivalent units (%). The HbA1cR Ratio is used to determine HbA1c results in IFCC equivalent units (mmol/mol). The required assays and parameter sheets are summarized in the following table:

Result Units	Photometric Assays	Ratio Assays
NGSP (%)	A1c_3 and tHb_3 HbA1c%	HbA1c%
IFCC (mmol/mol)	A1c_3 and tHb_3	HbA1cR

J. Substantial Equivalence Information:

1. Predicate device name: ADVIA® Chemistry Hemoglobin A1c Assay
2. Predicate K number: k081895
3. Comparison with predicate:

SIMILARITIES		
Item	ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment Assay (New Device)	ADVIA® Chemistry Hemoglobin A1c Assay (Predicate Device)
Intended Use	For *in vitro* diagnostic use in the quantitative determination of Hemoglobin A1c, a diabetes marker, in whole blood on the ADVIA Chemistry systems. Such measurements are used for monitoring the long-term care of persons with diabetes.	Same
Expected values	4–6% (20–42 mmol/mol)	Same
Format	Liquid, ready for use	Same
Sample Type	Human whole blood (lithium heparin or potassium EDTA)	Same
Calibrators	Siemens ADVIA® Chemistry A1c Calibrators	Same
Standardization	Traceable to International Federation of Clinical Chemistry (IFCC) and National Glycohemoglobin Standardization Program (NGSP)	Same
Analytical range	2.9-15.4% (8-144 mmol/mol)	Same
Reagent Storage Temperature	2-8°C	Same
DIFFERENCES		
Item	ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment Assay (New Device)	ADVIA® Chemistry Hemoglobin A1c Assay (Predicate Device)
Test Principle	**For Hemoglobin:** Measurement of released heme in the Soret region at 410 nm **For HbA1c:** Latex agglutination inhibition	**For Hemoglobin:** Conversion of all hemoglobin derivatives into alkaline hematin **For HbA1c:** Latex agglutination inhibition
Measurement Wavelength	A1c_3: 694 nm tHb_3: 410/694 nm	A1c: 694 nm tHb_2: 596 nm

K. Performance Characteristics

Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, method comparison, interfering substances and analytical range. All of the evaluation studies gave acceptable results compared to the predicate device. These

studies support that the ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment Assay is substantially equivalent to the ADVIA® Chemistry Hemoglobin A1c (A1c) Assay that is currently marketed.

I. Imprecision

Within run and Total Precision were established by assaying a normal whole blood sample and an abnormal whole blood sample. Each sample was assayed 2 replicates per run, 2 runs per day, for at least 20 days. Precision estimates were computed according to CLSI document EP05-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods*; Approved Guideline.

Sample	Level NGSP Units (%)	Standard Deviation NGSP Units (%)	Coefficient of Variation (%)	N
WITHIN RUN IMPRECISION				
Normal Control	5.45	0.07	1.3	80
Abnormal Control	8.70	0.06	0.7	80
TOTAL IMPRECISION				
Normal Control	5.45	0.13	2.4	80
Abnormal Control	8.70	0.14	1.6	80

Sample	Level IFCC Units (mmol/mol)	Standard Deviation IFCC Units (mmol/mol)	Coefficient of Variation %	N
WITHIN RUN IMPRECISION				
Normal Control	36	0.78	2.2	80
Abnormal Control	71	0.67	0.9	80
TOTAL IMPRECISION				
Normal Control	36	1.41	3.9	80
Abnormal Control	71	1.47	2.1	80

II. Linearity/assay reportable range:

A linearity study across the entire measuring range was assessed using commercially available linearity set solutions. The low and high levels of the linearity set were mixed to make nine (9) intermediate levels and all samples were tested on the ADVIA Chemistry 1800 analyzer. The range of samples tested was from 1.13-19.44% A1c. The observed values were compared to the expected values.

Linear/measuring range of the assay is

- The A1c_3 assay can be used for specific A1c concentrations from 1.0 to 8.83 µmol/L.
- The tHb_3 assay can be used for total hemoglobin concentrations from 7 to 24 g/dL.
- The HbA1c% assay is linear from 2.9 to 15.4% HbA1c.
- The HbA1cR assay is linear from 8 to 144 mmol/mol.

The low end of the assay range is calculated based on the Limit of Detection. The high end of the assay range is based on the linearity calculation.

III. Limit of detection

The estimations of the Limit of Blank (LoB) and Limit of Detection (LoD) were performed by running 60 replicates of 0.9% Saline (Blank) and five (5) HbA1c low samples. Data were obtained from a 3-day precision study. The LoD for the HbA1c_3 assays is 0.48 µmol/L (0.91 %HbA1c).

IV. Method comparison with predicate device:

The performance of this method (y) on an ADVIA 1800 was compared with performance of ADVIA® Chemistry System A1c method (x). Ninety-eight (98) whole blood samples in EDTA were tested and the sample results ranged from 3.14 – 14.92 %HbA1c (11 – 139) mmol/mol) and gave a correlation coefficient of 0.9942.

Linear regression analysis gave the following equation:
This method = 1.00 (predicate device) – 2.90 mmol/mol

IV. Analytical specificity

Interferences from icterus, lipemia, and hemolysis were evaluated for this Hemoglobin A1c method on an ADVIA 1800 analyzer using a significance criterion of >10% variance from the control. No significant lipemia interference was found at Intralipid levels from 0-1000 mg/dL in a 5.16%, 9.84% HbA1c sample. No significant interference was found at unconjugated bilirubin levels from 0-60 mg/dL in a 5.16%, 9.90% HbA1c sample. No significant interference was found at conjugated bilirubin levels from 0-60 mg/dL in a 5.03%, 9.78% HbA1c sample.

L. Conclusion:

The ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment assay is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Siemens Healthcare Diagnostics ADVIA® Chemistry Hemoglobin A1c Assay (k081895).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Silver Spring, MD 20993

Siemens Healthcare Diagnostics
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AUG 2 5 2011

Re: k110934
Trade Name: Advia 1800 Chemistry Hemoglobin A1C_3 Automated Pretreatment Assay
Regulation Number: 21 CFR §864.7470
Regulation Name: Glycosylated Hemoglobin Assay
Regulatory Class: Class II
Product Codes: LCP
Dated: July 29, 2011
Received: August 1, 2011

Dear Ms. White:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Courtney Harper, Ph.D.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K110934

Device Name: ADVIA® 1800 Chemistry Hemoglobin A1c_3 (A1c_3) Automated Pretreatment Assay

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Prescription Use X (21 CFR Part 801 Subpart D) And/Or Over the Counter Use (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K110934